

We claim:

1. A method of diagnosing or predicting susceptibility to a fibrostenotic subtype of Crohn's disease in a subject having Crohn's disease, comprising
5 determining the presence or absence of IgA anti-I2 antibodies in the subject,

wherein the presence of said IgA anti-I2 antibodies indicates that the subject has said fibrostenotic subtype of Crohn's disease.

10 2. The method of claim 1, further comprising determining the presence or absence in the subject of one or more fibrostenotic markers selected from a NOD2 variant, anti-Saccharomyces cerevisiae antibodies (ASCA), and anti-OmpC antibodies,

15 wherein the presence of said IgA anti-I2 antibodies or the presence of one of said one or more fibrostenotic markers each independently indicates that the subject has said fibrostenotic subtype of Crohn's disease.

20 3. The method of claim 2, wherein said one or more fibrostenotic markers is a NOD2 variant.

4. The method of claim 3, wherein said NOD2 variant is selected from R702W, G908R, and 1007fs.

25 5. The method of claim 2, wherein said one or more fibrostenotic markers is ASCA.

6. The method of claim 2, wherein said one or more fibrostenotic markers is IgA anti-OmpC antibodies.

7. The method of claim 2, wherein said one or more fibrostenotic markers are a NOD2 variant and ASCA.

8. The method of claim 1, wherein determining the presence or absence of IgA anti-I2 antibodies in the
5 subject comprises the steps of:

(a) contacting a sample from the subject with an I2 antigen, or immunoreactive fragment thereof, under conditions suitable to form a complex of I2 antigen, or immunoreactive fragment thereof, and antibody
10 against said I2 antigen;

(b) contacting said complex with a labeled secondary antibody; and

(c) detecting the presence or absence of said complex,

15 wherein the presence of said complex indicates the presence of said IgA anti-I2 antibodies in the subject.

9. The method of claim 1, further comprising determining the presence or absence of a NOD2 variant in
20 the subject,

wherein the presence of IgA anti-I2 antibodies and the presence of a NOD2 variant in the subject indicates that the subject has said fibrostenotic subtype of Crohn's disease.

10. The method of claim 9, wherein the combined presence of said IgA anti-I2 antibodies and said NOD2 variant in the subject is associated with said fibrostenotic subtype of Crohn's disease with an odds
5 ratio of at least 6.

11. The method of claim 1, further comprising determining the presence or absence of ASCA in the subject,

wherein the presence of said IgA anti-I2
10 antibodies and the presence of said ASCA in the subject indicates that the subject has said fibrostenotic subtype of Crohn's disease.

12. The method of claim 11, wherein the combined presence of said IgA anti-I2 antibodies and said
15 ASCA in the subject is associated with said fibrostenotic subtype of Crohn's disease with an odds ratio of at least 6.

13. The method of claim 9, further comprising determining the presence or absence of said ASCA in the
20 subject,

wherein the combined presence of IgA anti-I2 antibodies, said NOD2 variant, and said ASCA in the subject indicates that the subject has said fibrostenotic subtype of Crohn's disease.

25 14. The method of claim 13, wherein the combined presence of said IgA anti-I2 antibodies, said NOD2 variant, and said ASCA in the subject is associated with said fibrostenotic subtype of Crohn's disease with an odds ratio of at least 9.

15. A method of diagnosing or predicting susceptibility to a clinical subtype of Crohn's disease in a subject having Crohn's disease, comprising determining the presence or absence of IgA anti-I2
5 antibodies in the subject,

wherein the presence of said IgA anti-I2 antibodies indicates that the subject has a clinical subtype of Crohn's disease.

16. The method of claim 15, wherein said
10 clinical subtype of Crohn's disease is a fibrostenotic subtype of Crohn's disease.

17. The method of claim 15, wherein said clinical subtype of Crohn's disease is characterized by the need for small bowel surgery.

15 18. The method of claim 15, wherein said clinical subtype of Crohn's disease is characterized by the absence of features of ulcerative colitis.

19. The method of claim 15, further comprising determining the presence or absence in the subject of one
20 or more markers selected from a NOD2 variant, anti-Saccharomyces cerevisiae antibodies (ASCA), IgA anti-OmpC antibodies, and perinuclear anti-neutrophil cytoplasmic antibodies (pANCA).

20. The method of claim 19, wherein said one
25 or more markers is a NOD2 variant.

21. The method of claim 20, wherein said NOD2 variant is selected from R702W, G908R, and 1007fs.

22. The method of claim 19, wherein said one or more markers is ASCA.

23. The method of claim 19, wherein said one or more markers are a NOD2 variant and ASCA.

5 24. The method of claim 15, wherein determining the presence or absence of IgA anti-I2 antibodies in the subject comprises the steps of:

(a) contacting a sample from the subject with an I2 antigen, or immunoreactive fragment thereof,
10 under conditions suitable to form a complex of I2 antigen, or immunoreactive fragment thereof, and antibody against said I2 antigen;

(b) contacting said complex with a labeled secondary antibody; and

15 (c) detecting the presence or absence of said complex,

wherein the presence of said complex indicates the presence of said IgA anti-I2 antibodies in the subject.

25. A method of determining a risk of having or developing a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery in a subject
5 having Crohn's disease, comprising determining the presence or absence of three markers in the subject,

said three markers being IgA anti-I2 antibodies, anti-*Saccharomyces cerevisiae* antibodies (ASCA), and IgA anti-OmpC antibodies,

10 wherein the presence of said three markers indicates a first risk of having or developing said clinical subtype of Crohn's disease, the presence of exactly two of said three markers indicates a second risk of having or developing said clinical subtype of Crohn's
15 disease, the presence of exactly one of said three markers indicates a third risk of having or developing said clinical subtype of Crohn's disease, and the absence of said three markers indicates a fourth risk of having or developing said clinical subtype of Crohn's disease,

20 and wherein said first risk is greater than said second risk, said second risk is greater than said third risk, and said third risk is greater than said fourth risk.

26. A method of determining a risk of having
or developing a clinical subtype of Crohn's disease
characterized by the need for small bowel surgery in a
subject having Crohn's disease, comprising determining
5 the presence or absence of three markers in the subject,

said three markers being IgA anti-I2
antibodies, anti-*Saccharomyces cerevisiae* antibodies
(ASCA), and IgA anti-OmpC antibodies,

wherein the presence of said three markers
10 indicates a first risk of having or developing said
clinical subtype of Crohn's disease, the presence of
exactly two of said three markers indicates a second risk
of having or developing said clinical subtype of Crohn's
disease, the presence of exactly one of said three
15 markers indicates a third risk of having or developing
said clinical subtype of Crohn's disease, and the absence
of said three markers indicates a fourth risk of having
or developing said clinical subtype of Crohn's disease,

and wherein said first risk is greater than
20 said second risk, said second risk is greater than said
third risk, and said third risk is greater than said
fourth risk.

27. A method of determining a risk of having or developing a clinical subtype of Crohn's disease in a subject having Crohn's disease, said clinical subtype characterized by fibrostenosis or the need for small
5 bowel surgery, said method comprising

determining the presence and magnitude of IgA anti-I2 antibody response in the subject,

wherein a greater magnitude of IgA anti-I2 antibody response indicates a greater risk of having or
10 developing said clinical subtype characterized by fibrostenosis or the need for small bowel surgery.

28. A method of determining a risk of having or developing a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating
15 disease or the need for small bowel surgery in a subject having Crohn's disease, comprising

determining the presence and magnitude of IgA anti-OmpC antibody response in the subject,

wherein a greater magnitude of IgA anti-OmpC
20 antibody response indicates a greater risk of having or developing said clinical subtype characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery.

29. A method of determining a risk of having or developing a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery in a subject
5 having Crohn's disease, comprising determining the presence and magnitude of three markers in the subject,

said three markers being IgA anti-I2 antibodies, anti-*Saccharomyces cerevisiae* antibodies (ASCA), and IgA anti-OmpC antibodies,

10 wherein a greater magnitude of said three markers combined indicates a greater risk of having or developing said clinical subtype characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery.